Remarks

Claims 15, 16, 21-24, 26 and 27, all Claims that were pending, have been cancelled. Claims 28-32 have been added. The Claims are supported by the previous Claims. Claim 28 is supported at least at original Claim 1 of the present application, and by Claim 1 of the parent patent. Claims 29 and 31 are supported at least at original Claim 16; Claims 30 and 31 are supported at least at original Claim 20, and at page 24, line 8. Claim 32 is supported at least at original Claim 21. In light of new matter objections, amendments to the paragraphs bridging pages 22-23 and 23-24 of the present application have been withdrawn. A new amendment to the paragraph bridging pages 23-24 is submitted solely to correct an obvious typographic error.

This application is a CIP of an allowed patent, and incorporates all the limitations of Claim 1 of the parent patent. The Examiner made a restriction requirement in the case with respect to the added limitations, and made it final. The applicants filed an RCE and requested a broader search, which was denied.

Election/Restrictions

This application contains claims 15, 16 and 21 drawn to an invention nonelected with traverse in the paper filed 5-12-03. The Examiner states that a complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 15, 16 and 21 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 15, 16 and 21 have been mislabeled as "currently amended" in the amendment filed 12-&04. In the future, the claims should be labeled as "withdrawn"

The original restriction/election was limited to administering the patentably distinct combination of ddl (an RT inhibitor) and indinavir (a protease inhibitor). The restriction is being maintained because i) RT inhibitors, protease inhibitors and hydroxyurea have different structures and functions, ii) the species of RT inhibitors in claims 24 and 26 have different structures and inhibit RT using different mechanisms, iii) the species of protease inhibitors in claims 25 and 27 have different structures and inhibit protease using different mechanisms, and ii) the burden required to search administering all combinations of RT inhibitor species and protease inhibitor species together with administering DNA encoding an immunogenic retroviral protein would be undue.

Claims 22-24, 2 and 27 are only under consideration as they relate to administering antiretroviral drug therapy comprising ddl (an RT inhibitor) and indinavir (a protease inhibitor) until viral replication is suppressed, and then administering DNA encoding an immunogenic retroviral protein operably linked with a promoter. Applicants' request for searches of other aritiviral drugs has been denied.

Response – Restriction/election Requirement

In response the Applicants note that all Claims have been cancelled, and new Claims are submitted. This application is a CIP of USPN 6,420,176. The Claims have been amended to quote all the limitations of Claim 1 of the parent patent. The Claims all include further limitations to the parent patent. The Examiner has admitted there is no prior art against the Claims, yet has refused to broaden the scope of search, even after an RCE with a request for a broadened search was filed.

Specification

The Examiner states that the status of US Patent Applications on pg 4, line 28, pg 11, line 23, and pg 16,line 29, needs updated as necessary.

The Examiner states that the amendment filed 3/11/04 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material that is not supported by the original disclosure is as follows: the specification does not support the changes made to the paragraph bridging pg 22-23 or the paragraph bridging pg 23-24.

The Examiner states that "Applicant is required to cancel the new matter in the reply to this Office Action. Applicants argue "Gilead Sciences (formerly, Gilead pharmaceuticals) uses the trade name Preveon® for a drug known variously as adefovir, adefovir dipioxil and PMEA, the trade name Viread® for the drug know as tenofovir, tenofovir DF and PMPA; Glaxo Wellcome is now GlaxosmithKline; efavirenz (Sustiva®) was once owned by Dupont and is now owned by Bristol-Myers Squibb; lubocavir developed safety issues and is no longer available, and so has been deleted. Similarly, with respect to the paragraph bridging pages 23-24, Nelfinavir (Viracept®) has been available overseas from Roche, but is available from Auguoron in the US now. GWI 41, formerly available from Glaxo Wellcome/vertex, is no longer available and has been deleted, Tipranavir, formerly available from Pharmacia & Upjohn, is now available from Boehringer. An altemate generic drug name, atazanavir, and a trade name, Reyataz® have come into use for a Bristol-Myers Squibb material, BMS 232632." Applicants' argument is not persuasive. Unless the names were known at the time of filing, the trade names are new matter. Deleting drugs that are no longer available or that developed safety issues is new matter."

Response – Specification

In response, the Applicants cancel the prior to amendments, with the exception of an obvious typographic error.

Claim Rejections – 35 USC § 112 – Enablement

Claims 22-24, 26 and 27 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for reasons of record.

The Examiner considers administering an antiretroviral drug therapy comprising ddl and Indinavir until retroviral replication is effectively suppressed because Finzi taught

administering a reverse transcriptase inhibitor and a protease inhibitor suppressed retroviral replication (Finzi et al. Science. Nov. 14, 1997, Vol. 278, pg 1295-1300).

Claims 22-24, 26 and 27 are said to require administering DNA encoding an immunogenic retroviral protein after administering the antiretroviral drug therapy. The Examiner says that the sole disclosed purpose for administering DNA encoding an immunogenic retroviral protein is to induce an immune response against the retroviral protein that is therapeutic (pg 2, lines 14-19). Therefore, the Examiner states that the step of administering DNA encoding an immunogenic retroviral protein must be fully enabled for using the DNA to obtain a therapeutic immune response against the "immunogenic retroviral protein". However, the Examiner states that the specification does not enable using DNA encoding an immunogenic retroviral protein to induce a therapeutic immune response against a retrovirus in a host.

The Examiner takes the position that Claims 22-24, 26 and 27 are not enabled because the structure of the DNA encoding an immunogenic retroviral protein that provides a therapeutic immune response against the retroviral protein is not enabled. The Examiner states that, according to another reference, not the inventor's disclosure, that the state of the art at the time of filing was that the combination of vector, promoter, route of administration, level of expression and target tissue required to obtain a therapeutic or prophylactic effect using gene therapy was unpredictable. Millerof record (1995, FASEB J., Vol. 9, pages 190-199) review the types of vectors available for in vivo gene therapy, and conclude that "for the long-term success as well as the widespread applicability of human gene therapy, there will have to be advances... targeting strategies outlined in this review, which are currently only at the experimental level, will have to be translated into components of safe and highly efficient delivery systems" (page 198, column 1). Deonarain of record (1998, Expert Opin. Ther. Pat., Vol. 8, pages 53-69) indicate that one of the biggest problems hampering successful gene therapy is the "ability to target a gene to a significant population of cells and express it at adequate levels for a long enough period of time" (page 53, first paragraph). Deonarain reviews new techniques under experimentation in the art that show promise but states that such techniques are even less efficient than viral gene delivery (see page 65, first paragraph under Conclusion section). Verma of record (Sept. 1997, Nature, Vol. 389, pages 239-242) reviews vectors known in the art for use in gene therapy and discusses problems associated with each type of vector. The teachings of Verma indicate a resolution to vector targeting has not been achieved in the art (see entire article). Verma also teaches appropriate regulatory elements may improve expression, but it is unpredictable what tissues such regulatory elements target (page 240, sentence bridging columns 2 and 3). Crystal of record (1995, Science, Vol. 270, page 404410) also reviews various vectors known in the art and indicates, "among the design hurdles for all vectors are the need to increase the efficiency of gene transfer, to increase target specificity and to enable the transferred gene to be regulated" (page 409).

The Examiner says that the state of the art regarding treating retroviral infection was unpredictable, that Stricker of record (Medical Hypotheses, June 1997, Vol. 48, pages 527-9) teaches that attempts to develop a vaccine against HIV have been unsuccessful because HIV vaccines do not neutralize HIV (pg 527, last paragraph through all of pg 528). Overall, a lack of understanding about protective immunity to HIV in humans, the sequence variability of HIV and the rapid replication of HIV contribute the ineffectiveness of vaccines against HIV (Bangham of record, Nov. 29, 1997, Lancet, Vol. 350, pages 1617-1621; page 1617, top of col. 1).

The Examiner admits that the specification teaches a complex comprising i) manosylated PEI and ii) DNA encoding an immunogenic HIV protein operably linked to a promoter. The Examiner remarks that administration of the complex to a host after drug therapy was followed by an increase in CD4 cells then a decrease in CD4 cells (pg 53). The Examiner concludes that the specification does not provide adequate guidance for one of skill to use DNA encoding an "immunogenic retroviral protein" to induce an immune response capable of treating a retroviral infection. The Examiner discounts the results

described in the specification as being not therapeutic because the overall result does not result in a net increase in CD4 cells. In addition, the Examiner states that it cannot be concluded that the DNA encoding a retroviral protein caused the initial increase in CD4 cells because the experiment did not include controls - animals that did not receive drug therapy or the gene complex. The Examiner says the specification does not provide adequate guidance indicating the increase in CD4 was caused by an immune response to the retroviral protein encoded by the DNA - the drug therapy could have caused the increase in CD4. The specification did not teach treating animals that were already infected or challenging the animals after they were given DermaVir. For administration of DNA encoding a retroviral protein to induce a therapeutic immune response, the specification must overcome the unpredictability in the art by adequately describing the structure of the foreign genetic material" used, the dosage and route of administration that results in a therapeutic effect or immunization." Without such guidance it would require one of skill in the art undue experimentation to overcome the unpredictability in the art regarding gene therapy and retroviral therapy to determine the combination of elements required to obtain a therapeutic or prophylactic effect against retroviral infection using "foreign genetic material. Therefore, the specification does not enable "therapeutic genetic immunization" using a gene delivery complex comprising"**foreign genetic material**" as claimed.

According to the Examiner, the Applicants argue, "the present invention, and a therapeutic response is described in the application in Example 13" (pg 7 of response filed 11-16-04). Applicants argue the application shows more than CD4 results. Applicants argue the application shows reduced viral replication, i.e. "a reduction in the rate of viral rebound when drug treatment was stopped after vaccination (pg 53, lines 22-27; Fig. 14)" (pg 9 of response).

Applicants' arguments regarding Example 13 are not persuasive. Example 13 has been addressed in the rejection above. In summary, it cannot be concluded that the DNA encoding a retroviral protein used in Example 13 caused an increase in CD4 cells because the experiment did not include controls - animals that did not receive drug therapy or the gene complex. Example 13 does not provide adequate guidance indicating the increase in CD4 was caused by an immune response to the retroviral protein encoded by the DNA - the drug therapy could have caused the increase in CD4. Example 13 did not teach treating animals that were already infected or challenging the animals after they were given DermaVir. Example 13 does not overcome the unpredictability in the art by adequately describing the structure of the "foreign genetic material" used or the dosage and route of administration that resulted in a therapeutic effect or "immunization" or that the DNA was responsible for any effect observed.

The Examiner says the Applicants' arguments regarding pg 53, lines 22-27, and the reduced viral replication described in the specification are not persuasive.
The specification states:

"The comparison of the rate of viral load rebound among those animals undergoing STI-HAART early after infection (Lori, F. et al. Control of Sly rebound through structured treatment interruptions during early infection. Science 290, 1591-1593. (2000)), those initiating STI-HAART during AIDS, and the same animals treated with STI-HAART plus DermaVirsHlv revealed an interesting pattern. The rate of viral rebound during consecutive HAART interruptions, that was unchanged before the initiation of vaccine therapy, decreased sharply after vaccination, and became remarkably similar to that observed in the animals treated with STI-HAART early after infection (Fig. 14). These results suggest that DermaVirSHIV therapy can improve the control of virus replication during interruption of HAART" (pg 53, lines 18-27). HAART therapy as described in Lori of record (2000) is PMPA (tenofovir, an RT inhibitor), ddl (didanosine, an RT inhibitor) and hydroxyurea(pg 1591, cot. 3, lines 10-18). STI-HAART is structured treatment interruptions of HAART therapy.

The examiner agrees that the interrupted administration of PMPA, ddl and hydroxyurea followed by administration of DermaVirsniv (AIDS(DermaVir)) in Fig. 14

shows decreased viral rebound as compared to interrupted administration of PMPA, ddl and hydroxyurea (AIDS(HAART)).

The Examiner states that the claims are being considered as they relate to administering ddl and indinavir followed by a gene complex; however, the example is limited to administering PMPA, ddl and hydroxyurea followed by a gene complex. The Examiner states that, in his view, the combination of administering drugs plus DermaVirSHIV in the example does not correlate to administering ddl and indinavir plus DermaVirSHIV. He speculates that the specific combination of DermaVirSHIV with PMPA or hydroxyurea may have decreased viral rebound in the example, or in the alternative that the combination of two different RT inhibitors in the example with DermaVirsHIv decreased viral rebound (PMPA and ddl have different structures and different mechanisms of action (see DeClercq, Current Medicinal Chemistry, 2001, Vol. 8, pg 1543-1572; bridging pg 1553-1554; nucleotide vs. nucleoside analogues; (PMPA only needs two phosphorylation steps to be converted to the active metabolite"). The Examiner states that the example does not use indinavir or any other protease inhibitor. The Examiner suggests that the decreased viral rebound effect in the example may be a synergistic effect obtained only in the presence of PMPA, PMPA and ddl, or hydroxyurea.

Therefore, the Examiner concludes that one of skill would not expect DermaVirsHIv to decrease viral rebound after administering ddl and indinavir based on the example, which is limited to administering ddl, PMPA and hydroxyurea followed by DermaVirSHIV.

Furthermore, the Examiner states that the claims encompass administering continuous HAART followed by DermaVirsH,V; however, the example is limited to interrupted HAART. The Examiner states that the specification does not correlate decreasing viral rebound obtained by interrupting HAART followed by DermaVirsHrv with expected results obtained by administering continuous HAART plus DermaVirSHIV (i.e. the virus does not rebound during continuous HAART). On this basis, the Examiner contends that the mode of drug delivery in the example does not correlate to any mode of delivery as broadly encompassed by claim 21. The claims are said to encompass delivering any gene complex comprising DNA encoding any immunogenic retroviral protein; however, the example is limited to DermaVirSHIV.

The Examiner quotes the specification as saying:

"DermaVirSHIV is a glucose-water solution containing a plasmid DNA as an active ingredient and polyethylenimine-mannose (PEIm) as an adjuvant (See Example 12). One therapeutic application contained 01 mg DNA capable of expressing all but the integrase protein of the Simian-Human Immunodeficiency Virus (SHIV). DermaVirSHIV was formulated to transduce Langerhans cells located in the epidermis and it was applied on the surface of the skin of the animals. We have shown that these Langerhans cells are triggered to migrate to the lymph nodes, mature to dendritic cells and present SHIV antigens to naive T cells. After SHIV-specific activation of naïve I cells in the lymph nodes, DermaVirSHIV initiated potent SIV-specific I cell-mediated immune responses in uninfected monkeys (See Example 12)" (pg 52, lines 1-9).

The Examiner states the specification does not correlate the results obtained with DermaVirsHIv, which expresses all retroviral proteins except integrase, to any DNA encoding any immunogenic retroviral protein as broadly claimed, specifically DNA encoding one immunogenic retroviral proteins, such as gpl 20. The Examiner states, that expression of all retroviral proteins may be essential to induce the proper immune response and decrease viral rebound. (see pg 52, lines 19).

The Examiner states that, not only is the gene complex itself much narrower in scope than the gene delivery complex claimed, the mode of delivery described in the specification is limited to dermal administration.

In conclusion, the Examiner states that the example on pg 53 is much narrower than claim 21 in the types of drugs administered, the mode of delivery of the drugs, the gene complex being delivered and the mode of delivery of the gene complex. The Examiner states that decreasing viral rebound after interrupting two RT inhibitors and hydroxyurea

cannot even be extrapolated to administration of ddI and indinavir because the combination of drugs in the example may have allowed DermaVirSHIV to function.

Response – Claim Rejections 35 USC § 112 – enablement

The Examiner appears to be operating under a misunderstanding of the applicable law. The disclosure in a patent application is required to enable one skilled in the art to make or use the claimed invention. There is no requirement for an inventor to conform to somebody else's idea of what might be required. Further, all the disclosure of the application must be relied upon for enablement of the invention, and not just the specific examples used to illustrate the invention. The Claims are not limited merely to the specific materials used in the Examples. In addition, the Examiner appears to be operating under a misunderstanding of fact: a therapeutic immune response is unquestionably demonstrated in the text.

Thus, the drugs that are enabled by this application are enabled because of the disclosure in this application, at least at pages 21-24. This happens to be consistent with the Finzi reference cited by the Examiner, but the enabling disclosure belongs to the Applicants.

With respect to the Miller, Deonarain, Verma, Crystal, etc., references cited of record, the Examiner has cited a laundry list of requirements that those authors, not the inventors, thought would be needed for the present invention. Those authors were wrong, and that is one reason why they are not the inventors of the present case.

The Examiner admits that the specification teaches a complex comprising I) mannosylated PEI and DNA encoding an immunogenic HIV protein operably linked to a promoter, but the Examiner says the Experiment 13 does not describe a therapeutic effect, because an increase in CD4 cells was followed by a decrease in CD4 cells. Example 13 reports that the inventors were interested in controlling viral replication (page 49, lines 19-27), and so the Figures 11, 12 and 13 report numbers of copies of virus in the blood. The effect of drug treatment until viral load is suppressed, followed by vaccination, on viral replication is unmistakable. Viral replication was suppressed. The paragraph cited by the Examiner notes that questions the value of CD4 cell numbers as a surrogate marker for immune system effectiveness. It notes that CD4 counts fluctuated during the experiment, generally increasing after treatment, and decreasing when viral rebound occurred, links the widest swings in CD4 count with the animal who had the highest viral load rebounds, and noted that among the rest of the animals, the animal with the lowest CD4 count was the first to achieve control of viral load during treatment interruptions. The application suggests that a low number of CD4 T lymphocytes might contribute to the control of the virus production during the treatment interruption cycles, and notes that others have reached similar conclusions about CD4 counts, citing an article from the New England Journal of Medicine.

The Examiner's statement that the specification did not teach treating animals that were already infected is mistaken: it is clear from the text that all the animals treated with both drugs and the invented vaccine in experiment 13, were infected: they had virus in their blood. The Examiner is correct that this was not a challenge test. The Applicants note that a challenge test is used to measure the effectiveness of a preventive vaccine. In such a test, the vaccine is administered to healthy individuals who are then exposed to the disease. This applications describes a safety experiment that yielded surprising results. The vaccine was administered to individuals that were deathly ill. This experiment opens up a wholly new area of inquiry – the use of vaccines to treat already-infected individuals. A challenge test would have been irrelevant to the claimed invention.

The examiner's remarks with respect to "foreign genetic material" and "therapeutic genetic immunization" are believed to be a typographic error because the presently amended claims do not contain this language.

The examiner's comment with respect to controls – animals that did not receive drug therapy or the gene complex – is erroneous. The controls died long before this set of experiments were begun. See the application at page 50, lines 3-5. From the original cohort, 14 animals died prior to the study comparing continuous HAART and STI-HAART, and 3 more died during the protocol approval period. The remaining 7 were randomized into 3 receiving continuous HAART and 4 receiving STI-HAART. All the animals receiving continuous HAART died, similar to the experience in humans. See page 50, lines 12-22. The animals in the STI-HAART group had a better survival rate, but then they began to fail, as well. They began to show increasing viral load and viral rebound during treatment cessation periods See page 51, lines 12-18. This remnant population was used to test the vaccine. The application discloses that the inventors were interested in controlling viral replication. See page 51, lines 17-21, where the inventors disclose that they decided to study the potential benefit of vaccination in hopes of initiating specific T cell immunity, which has been previously shown to control virus replication in long-term non-progressors.

The Examiner states that there is no correspondence between the use of named drugs to suppress viral replication followed by vaccination, because the drugs have different structures and he speculates that the decreased viral rebound effect in the example may be a synergistic effect obtained only in the presence of PMPA, PMPA and ddI, or hydroxyurea. This possibility has been eliminated by the progression in the experiment. As discussed above, all the animals on continuous treatment had died, and the ones on drug treatment with planned interruptions had done better but were beginning to fail. The final experiment is a direct comparison between the best prior art treatment (STI-HAART) and the claimed invention (treatment until viral load is suppressed, then vaccinate) in the worst-case scenario

(animals near death). The effect of the vaccine on the animals cannot be attributed to the individual drug treatments, or to the treatment interruptions.

With respect to the description of the gene complex, the applicants note that the presently claimed complex is in fact narrower than that of the complex claimed in the parent patent No. 6,420,176:

> 1. A gene delivery complex comprising DNA and mannosylated polyethylenimine, wherein said DNA comprises a nucleic acid sequence encoding at least one immunogenic protein operatively linked to a promoter.

The applicants have amended the description of the gene delivery complex in the present case, which is a CIP of the parent where no text was deleted, to overcome formal objections by the Examiner and thereby facilitate prosecution:

28. (new) A method of treating retroviral infection, comprising
i) administering, to a host that is infected with a retrovirus, an antiretroviral therapy, until retroviral replication is suppressed, and then ii) administering a gene delivery complex comprising
a) DNA comprising a nucleic acid sequence encoding at least one immunogenic retroviral protein operably linked with a promoter and b) mannosylated polyethylenimine.

The Examiner has stated that the Example in the Specification does not correlate to the specification, so that the Claims are not enabled, apparently taking the position that the applicants are not entitled to claim the use of any given drug unless it is specifically supported by name (rather than class or function) *in an example*. However, these drugs are clearly disclosed and enabled in the application text. The drugs known to suppress viral replication, as claimed, are clearly disclosed by both class and function at least at page 21, lines 17-25. The names of various drugs that can be included in the claimed combinations are disclosed at least at pages 21, line 26-page 24, line 20, and the original Claims as filed. Hydroxyurea is specifically mentioned at least at original Claim 21. Reverse transcriptase inhibitors are disclosed at least at original Claim 19. Protease inhibitors are disclosed at least at original Claim 20. The applicants have submitted new Claims 28-31 that are supported at least by original Claims 19, 20 and 21. The applicants had attempted to update name and marketing information for various drugs, but the Examiner refused them, and the applicants have withdrawn the proposed changes.

The Prior Art

The Examiner states that Claims 22-24, 26 and 27 remain free of the prior art as they relate to administering antiretroviral drug therapy comprising ddI (an RI inhibitor) and

indinavir (a protease inhibitor) until viral replication is suppressed, and then administering a DNA complex comprising a) DNA encoding an immunogenic retroviral protein operably linked with a promoter; and b) mannosylated polyethylenimine. The Examiner admits that the prior art did not teach or suggest administering ddI and Indinavir until viral replication is effectively suppressed, and then administering a gene delivery complex as claimed. The Examiner notes that Finzi (Science. Nov. 14, 1997, Vol. 278, pg 1295-1300) taught administering reverse transcriptase inhibitors and protease inhibitors to HIV patients. However, the Examiner further comments that Finzi did not relate to administering DNA encoding the marker protein luciferase to the brain of mice as taught by Boussif (PNAS, Aug. 1995, Vol. 92. pg 7292-7301) of record, administering DNA encoding a marker protein to cells in vitro as taught by Zanta (Bioconjugate Chem. 1997. Vol. 8. pg 839844) of record, administering DNA encoding a marker protein to cells in vitro as taught by Behr (US Patent 6,013,240) of record, or administering virus encoding integrase defective HIV to cells in vitro as taught by Cara (Virology, 1995, Vol. 208, pg 242-248).

The Examiner adds that the claims have not been searched far other antiviral drugs in combination with the gene complex as requested.

Response – The Prior Art

The Applicants note that, an appropriately framed search of the combination of Indinavir and ddI in combination with the claimed vaccine would also reveal the use of Indinavir or ddI individually with the vaccine. If such prior art has been found, the applicants respectfully request its disclosure, as being closer than any of the presently cited art. If there is any other prior art relating to the use of the applicant's vaccine in combination with any other drug treatment, the applicants respectfully request that it be disclosed to them as soon as possible.

Double Patenting

The Examiner states that Claims 22-24, 26 and 27 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 6,420,176 in view of the disclosure of 6,420,176 for reasons of record. The claims of 176 are said to be directed toward a gene delivery complex comprising DNA encoding an immunogenic protein operably linked to a promoter and mannosylated polyethylenimine. The Examiner admits that the claims of the '176 patent do not require administration as required in the instant claims or administration of antiretroviral drug therapy. The Examiner, however, points out that MPEP 804 states the specification may be used as a dictionary to learn the meaning of a term in the patent claim. In this case, one of skill would look to the specification to determine the asserted utility of the product. The disclosure taught administering the gene delivery complex after suppressing viral replication using antiretroviral drug therapy (col. 12, lines 11-51, see especially lines 20-27). Thus, the Examiner asserts that it would have been obvious to one of ordinary skill in the art at the time the invention was made to administer the gene delivery complex in combination with drug therapy as claimed.

The Examiner acknowledges that the Applicants argue the instant application shows unexpected results over the '176 patent by showing "the unexpected therapeutic efficacy of DermaVir SHIV in animals at a late stage of the disease reveals a previously unsuspected capacity of the host to response to the vaccination" (pg 53, lines 28-31). The Examiner contends that the Applicants' argument is not persuasive. The Examiner says the statement on pg 53, lines 28-31, merely refers to interrupting administration of ddI, PMPA and hydroxyurea followed by dermal administration of DermaVirSHIV in mammals during late stages of AIDS. The Examiner says the statement cannot support an unexpected result for administering ddI+ indinavir followed by DermaVirSHIV or to the broad gene complex, mode of drug delivery, and mode of gene complex delivery encompassed by the claims. (This statement is not understood in the context of a double-patenting rejection, for it appears to be an enablement rejection of the present case over the parent. If the present case, which is a CIP of the parent is not enabled, it is difficult to see how it could possibly be rejected for double patenting over the parent.)

The Examiner states also that Claims 22-24, 26 and 27 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of copending Application No. 10/081922 for reasons of record. Although the Examiner admits the allegedly conflicting claims are not identical, he states that they are not patentably distinct from each other because they overlap in scope. Applicants argue '922 is a division of US Application 6,420,176 used in the obviousness-type double patenting rejection above. Applicants argue '922 is distinguished on the same basis. The Examiner states that Applicants' argument is not persuasive and has been addressed above.

Response – Double Patenting

The present application is a C-I-P of the cited US patent, and has the same inventive entity. The purpose of this rejection is not understood.

The Applicants also respectfully submit that the Examiner has overstated the disclosure in the parent patent. The statement in the patent text is more limited than the quote in the present rejection. At the time of the invention of the parent application, all well-known vaccines for infectious diseases except rabies were designed to be administered to healthy individuals. Even in the case of the rabies vaccine , the vaccine must be administered before the disease develops. That is because the mechanism for vaccine action depends on the stimulation of an existing capability within the body. If the body does not have the capability to mount a new immune response, the vaccine will not work. HIV destroys the immune system. By the time an individual has progressed to

AIDS, the immune system has been so substantially impaired that common, normally innocuous microbes cannot be kept in check. Thus, the suggestion at Col. 12, line 19, "If the replication of the wild-type virus can be suppressed *either before the immune system is substantially damaged or long enough to allow the immune system to recover*,[emphasis added] the present invention can be used to strengthen the immune system's ability to recognize the new variants of the virus...." represents the then-known limitations of the use of the vaccine. In other words, it was expected that, for the vaccine to have a therapeutic use, another condition or step would have to be added to first obtain an immune system capable of responding to the vaccine. Further, the Examiner admits only that it would have been "obvious to administer the gene delivery complex in combination with drug therapy as claimed" that is, to perform the experiment suggested in the parent patent, and points to no expectation of success without the disclosed intervening steps of 1) early diagnosis and treatment, or 2) treating with drugs until the immune system has recovered.

The Examiner also argues that the statement on pg 53, lines 28-31, merely refers to interrupting administration of ddI, PMPA and hydroxyurea followed by dermal administration of DermaVirSHIV in mammals during late stages of AIDS. The Examiner says the statement cannot support an unexpected result for administering ddI+ indinavir followed by DermaVirSHIV or to the broad gene complex, mode of drug delivery, and mode of gene complex delivery encompassed by the claims. This statement is not understood in the context of a double-patenting rejection, for it appears to be an enablement rejection of the present Claims over the present text. If the present case, which is a CIP of the parent is not enabled, and the enablement rejection has to do with subject matter introduced after the parent was filed, it is difficult to see how the claims could possibly be rejected for double patenting over the parent.

Conclusion

It is believed that all the Examiner's legitimate concerns have been met, and that the Claims are in condition for allowance. Favorable consideration is solicited.

Respectfully Submitted,

Valerie E. Looper

Valerie E. Looper
Registration No. 33,007